

## REMARKS

### Status of the claims

Claims 1-122 were originally presented with the application as filed. In a Preliminary Amendment mailed on July 23, 2002; claims 1-122 were cancelled and new claims 123-152 were added. Accordingly, claims 123-152 are presently pending in the application.

### Inventorship

Applicants again request that their petition for change in inventorship, mailed on November 21, 2002 (and a copy of which was mailed with Applicants December 17, 2003 Response), be acknowledged and reflected in an updated Filing Receipt.

### Claim interpretation

The Office interprets the term "library" to include any collection of nucleic acids. Final Office Action, page 2. This interpretation is incorrect. It is well-known in the art of molecular biology that a nucleic acid library is a collection of different nucleotide sequences. See, for example, Ausubel *et al.* (1987), copy attached as Exhibit A:

... a recombinant DNA library consists of a large number of recombinant DNA clones, *each one of which contains a different segment of foreign DNA.* (emphasis added)

See also Berger *et al.* (1987), copy attached:

A library is a mixture of clones constructed by inserting either cDNA or fragments of genomic DNA into a suitable vector. The term *library* implies the existence of large numbers of different recombinants ... (emphasis in original)

These art-recognized definitions make clear that a library is a collection of different sequences, not simply multiple copies of the same sequence. (Note that the latter definition states that a library is a *mixture of clones* and contains *a large number of different recombinants.*) Accordingly, the Office's interpretation of the term "library" is incorrect and, to the extent that the Office asserts that a library is nothing more than a set

of multiple copies of the same sequence (see *infra*), is repugnant to the normal meaning of the term in the art.

The Office Action further states: "A nucleic acid library is simply a cloned set of nucleic acids. So when Grosveld teaches cloning of the target nucleic acid into a vector, Grosveld is forming [a] 'library'." Final Office Action, page 9.

This statement, too, is incorrect. Cloning of "the target sequence" (*i.e.*, a single sequence) into a vector results in the production of multiple copies of the same sequence, or what is normally referred to in the art as a clone. It does not produce a library.<sup>1</sup>

### 35 U.S.C. § 103

The rejection over Grosveld (U.S. Patent No. 5,635,355) has been maintained for the reasons of record. The Office maintains its position that Grosveld discloses the construction of libraries of regulatory sequences, as claimed, and asserts that a finding of obviousness based on hindsight reconstruction is proper.

Applicants reiterate the remarks presented in their Responses of December 17, 2003 and February 26, 2004 and incorporate those remarks by reference herein.

Applicants maintain that Grosveld fails to disclose the construction of any type of library at all, let alone libraries of accessible sequences, as claimed. Rather, Grosveld discloses the construction of a clone of a DNA sequence, wherein the chromosomal copy of that DNA sequence, in certain cells, comprises a DNase hypersensitive site.

The Office also alleges that the specification does not define the term "library." This is yet another incorrect statement. The Examiner's attention is directed to page 46, lines 6-7, wherein it is stated: "As used herein, the term "library" refers to a pool of DNA fragments that have been propagated in some type of a cloning vector." Note the use of the plural "fragments" in the definition, indicating that a library is not defined as a collection of multiple copies of the same DNA fragment. See also page 47, lines 5-6: "The libraries formed can represent accessible regions for a particular cell type or cellular condition." Note the use of the plural "accessible regions." See also page 45, lines 7-8:

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<sup>1</sup> For a non-biological example, consider a building containing one million copies of the same book. A reasonable person would not consider such a building to be a library.